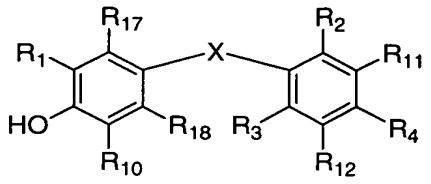
THYROID RECEPTOR LIGANDS

ABSTRACT OF THE DISCLOSURE

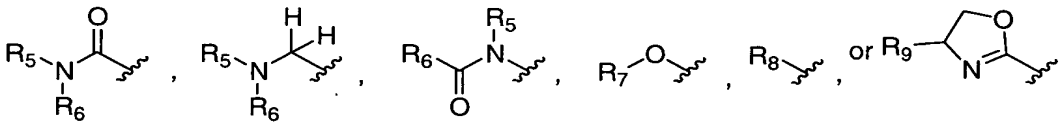
Thyroid receptor ligands are provided which have the general formula I



I

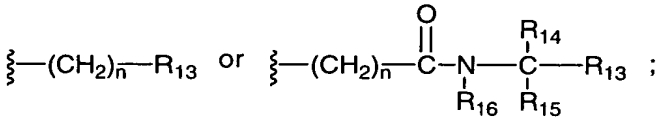
wherein:

R1 is



R2 and R3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, provided that at least one of R2 and R3 is other than hydrogen;

R4 is



R5 and R6 are the same or different and are selected from hydrogen, aryl, heteroaryl, alkyl, cycloalkyl, aralkyl or heteroaralkyl.

R7 is aryl, heteroaryl, alkyl, aralkyl, or heteroaralkyl;

R8 is aryl, heteroaryl, or cycloalkyl;

R9 is R7 or hydrogen;

R10 is hydrogen, halogen, cyano or alkyl;

R11 and R12 are each independently selected from the group consisting of hydrogen, halogen, alkoxy, hydroxy (-OH) cyano, and alkyl;

R13 is carboxylic acid (COOH) or esters thereof, phosphonic and phosphinic acid or esters thereof, sulfonic acid, tetrazole, hydroxamic acid, thiazolidinedione, acylsulfonamide, or other carboxylic acid surrogates known in the art;

R14 and R15 may be the same or different and are selected from hydrogen and alkyl, or R14 and R15 may be joined together forming a chain of 2 to 5 methylene groups [-(CH2)m-, m = 2, 3, 4 or 5], thus forming 3- to 6-membered cycloalkyl rings;

R16 is hydrogen or alkyl of 1 to 4 carbons;

R17 and R18 are the same or different and selected from hydrogen, halogen and alkyl;

n is 0 or an integer from 1 to 4;

X is oxygen (-O-), sulfur (-S-), sulfonyl (-SO_2-), sulfenyl (-SO-) selenium (-Se-), carbonyl (-CO-), amino (-NH-) or methylene (-CH2-); wherein the substituents are as described herein.

In addition, a method is provided for preventing, inhibiting or treating diseases or disorders associated with metabolism dysfunction or which are dependent upon the expression of a T_3 regulated gene, wherein a compound as described above is administered in a therapeutically effective amount.